Remarks

Claims 1, 3-34, 55-58, 60-63 and 65-73 were pending. Claims 1, 14, and 55 have been amended. Claims 60-62, 65-68, 71 and 73 have been canceled. The Applicants expressly reserve the right to prosecute unelected claims, canceled claims, claims to subject matter removed from any pending claim during prosecution, and claims to disclosed but unclaimed subject matter in one or more subsequent patent applications claiming the benefit of priority to the instant application. 35 U.S.C. §§ 120, 121.

Specification

The Examiner asserts that the Specification of the present application is missing and requests that Applicant resubmits a copy of Specification as originally filed. In compliance with the Examiner's request, Applicant includes herewith a copy of the Specification as originally filed.

Claim Rejections - 35 U.S.C. § 102(e)

Claims 1-3, 13-16, 18-19, 24, 31-34, 55-58, 60-63, 65-67, and 69-72 stand rejected under 35 U.S.C. § 102(e) as being anticipated by US Patent No. 6,287,290 to Perkins et al. ("Perkins"). The Applicant respectfully traverses the rejection.

To anticipate a claim under §102, a reference must teach each and every element of the claim, either expressly or inherently. M.P.E.P. § 2131. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union oil Co. of California,* 8144. F. 2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Furthermore, "[t]he identical invention must be shown in as complete detail as contained in the … claim." *Richardson v. Suzuki Motor Co.,* 868 F.2d 1226, 1236, 9 U.S.P.Q.2d 1566 (Fed. Cir. 1990). Applicant submits that the cited art does not meet this standard.

The Examiner asserts that Perkins discloses "introducing material (gases/liquids/fibrin) through the bronchoscope into a diseased alveolar region within the targeted region." *Office Action* at page 2. However, the Applicant respectfully contends that the methods for lung volume reduction disclosed in Perkins do not target the alveolar region of the lung. Perkins

teaches optionally sealing or occluding an air passage leading to the collapsed region of the lung by "delivering a plug…, typically at [*sic*] partially hydrated collagen hydrogel…" ***after*** the lung has been collapsed by vacuum aspiration or the application of external force. The plug is delivered to the lung bronchus and used to seal the air passage leading to the target lung segment. *See Perkins*, column 9, lines 24-29; column 10, lines 37-58; and Figure 4C. Importantly, Perkins defines an "air passage" as a "segment of the branching bronchus which deliver[s] to and receive[s] air from the alveolar regions of the lung." *Perkins*, column 6, lines 34 -39.

In light of the explicit definition of "air passage" in Perkins, a summary of human pulmonary anatomy is appropriate, in support of which the Applicant respectfully directs the Examiner to Exhibit A (Figure 1-2) depicting a schematic diagram of the human airway. As shown in Exhibit A, the left and right bronchi are the two main tubes of the lung that extend from the trachea and branch off within the lung to form secondary and tertiary bronchi. The bronchi further branch to form smaller bronchioles and terminal bronchioles. At the ends of the terminal bronchioles are the alveoli. Based on the explicit definition of "air passage" in Perkins, the Applicant respectfully asserts that the methods of Perkins are limited to sealing the lung at the bronchi before the lung branches into its substructure.

In contrast, the Applicant's claimed methods relate to reducing lung volume in a patient by introducing material through a bronchoscope into a diseased alveolar region within the targeted region where the material induces collapse of the targeted region, promotes adhesion between one portion of the lung and another, and promotes fibrosis in or around the collapsed region of the lung. Thus, in the claimed methods the material does not serve merely as a plug to ***occlude*** the air passage leading to the collapsed tissue region as in Perkins, but acts to induce collapse, promote adhesion, and promote fibrosis. (*Specification* at page 1, lines 31 to page 2, lines 1-9.)

Critically, Perkins does not explicitly or inherently disclose promoting stable volume reduction of a targeted region of a patient's lung by introducing a material through a bronchoscope into a diseased alveolar region within the targeted region where the material induces collapse of the targeted region, promotes adhesion between one potion of the lung and

another and promotes fibrosis in or around the collapsed region of the lung. Thus, Perkins does not expressly or inherently teach each and every element of Applicant's claims.

Therefore, Applicant respectfully requests the withdrawal of the claim rejections under 35 U.S.C. § 102(e).

Claim Rejections - 35 U.S.C. § 103(a)

Legal Standard for Obviousness

To establish a *prima facie* case of obviousness, a number of criteria must be met. For example, all of the limitations of a rejected claim must be taught or suggested in the prior art reference (or references when combined) relied upon by the Examiner; or they must be among the variations that would have been "obvious to try" to one of ordinary skill in the relevant art in light of the cited reference(s). Moreover, one of ordinary skill in the relevant art must have a reasonable expectation of success in light of the cited reference or combination of references. Importantly, the reasonable expectation of success must be found in the prior art, and may not be based on the Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991); see MPEP § 2143 - § 2143.03 for decisions pertinent to each of these criteria.

Perkins

Claims 6-12 and 28 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Perkins. The Applicant respectfully traverses the rejection.

Narrow Scope of Perkins Disclosure

As discussed above, the methods of Perkins are limited to sealing the lung at the structural level of the bronchi, as opposed to at the level of the alveolar region as claimed by Applicant.

Patentability of Amended Claims

The criteria for establishing a prima facie case of obviousness are outlined above. In stark contrast to the disclosure of Perkins and what would have been "obvious to try" in light thereof, the Applicant's claimed methods relate to reducing lung volume in a patient introducing a material through a bronchoscope into a diseased alveolar region within the targeted region,

where the material induces collapse of the targeted region, promotes adhesion between one potion of the lung and another, and promotes fibrosis in or around the collapsed region of the lung.. The portion of the lung targeted in Applicant's claimed methods is the ***alveolar region*** (i.e., the region at the end of the terminal bronchioles).

Importantly, Perkins does not teach or render "obvious to try" performing lung volume reduction by introducing a material into the alveolar region of the lung; inducing collapse of the targeted region; promoting adhesion between one collapsed portion of the lung and another; and promoting fibrosis in or around the collapsed region. Rather, Perkins discloses the use of a plug delivered to the lung ***bronchus*** to occlude the "air passage" leading to the collapsed tissue region, wherein the region has previously been collapsed by the application of an external force or vacuum aspiration of the air contained in that region of the lung. In other words, Perkins teaches a method in which a region of the lung is first collapsed, followed by occlusion of an "air passage." Moreover, the Applicant respectfully contends that the numerous and substantial distinctions between the claimed methods and the teachings of Perkins are beyond the scope of the variations that the Examiner may reasonably characterize as "obvious to try" to one of ordinary skill in the relevant art in light of Perkins. For example, the differences between the claimed methods and the teachings of Perkins cannot reasonably be described as merely selecting a particular species from a well-defined genus of limited scope. Nor can those same differences be reasonably characterized as the result of nothing more than routine experimentation or refinement of what was known in the art.

Further, one of ordinary skill in the art would not have had a reasonable expectation of success in developing the claimed lung volume reduction methods in light of Perkins. Due to their understanding of "collateral ventilation" those of ordinary skill in the relevant art at the time the instant application was filed did not view the methods for lung volume reduction disclosed by Perkins as effective in producing atelectasis, and preventing the targeted region of the lung from receiving air flow. Collateral ventilation is the pulmonary phenomenon whereby apparently isolated alveolar regions are ventilated through passages or channels that bypass standard airways. As a result of collateral ventilation, a section of a lung targeted for volume reduction via occlusion at the level of an "air passage" as defined in Perkins still receives airflow due to the presence of auxiliary airways, thereby preventing atelectasis.

Submitted herewith is Exhibit B, visually underscoring some of the pertinent structural and therapeutic distinctions between normal lung tissue and emphysematous lung tissue with collateral ventilation. Exhibit B consists of four illustrations: normal lung tissue; emphysematous lung tissue with collateral ventilation into which a bronchial plug has been inserted; emphysematous lung tissue with collateral ventilation into the alveolar regions of which a composition comprising a protease has been introduced; and the resulting reduction in volume of the emphysematous lung tissue after such protease treatment. Accordingly, the Applicant respectfully contends that one of ordinary skill in the art would not have had a reasonable expectation of success in developing the claimed lung volume reduction methods in light of Perkins.

In further support of this analysis, Applicant includes herewith two references, marked as Exhibits C and D, which discuss the highly problematic effects of collateral ventilation in bronchoscopic lung volume reduction therapy. The references disclose that collateral ventilation prevents atelectasis in bronchoscopic lung volume reduction when the lung is occluded in the bronchial portion of the airway (i.e., at the level of an "air passage" as defined in Perkins). In other words, the references establish that methods like those disclosed in Perkins are generally ineffective in achieving lung volume reduction.

Consequently, the Applicant respectfully contends that one of ordinary skill in the art would not have had a reasonable expectation of success in utilizing the methods disclosed in Perkins for lung volume reduction. Moreover, the Applicants respectfully contend that the teachings of Perkins and the Exhibits provided herewith would have led one of ordinary skill in the art to conclude that it would be *unreasonable* to expect success in developing the claimed methods. Accordingly, the Applicants respectfully assert that no colorable argument can be made that one of ordinary skill in the art would have had a reasonable expectation of success in developing the claimed methods for lung volume reduction at the time the instant application was filed.

Based on the foregoing, Applicant respectfully requests withdrawal of the claim rejections under 35 U.S.C. § 103(a) based on Perkins.

Perkins in view of Edwardson

Claims 4-5, 17, 20-21, 26-27, 29-30, 68, and 73 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Perkins in view of US Patent No. 5,739,288 to Edwardson et al. ("Edwardson"). The Applicant respectfully traverses the rejection.

First, the Applicant respectfully disagrees with the Examiner's contention that Applicant has attempted to "show non-obviousness by attacking the cited references individually where the rejection is based on a combination of references." *Office Action* at page 6. Rather, the Applicant asserts that the skilled artisan would not arrive at the claimed invention based on the combination of Perkins and Edwardson because the cited combination does not disclose or render "obvious to try" all of the limitations of the rejected claims.

As discussed above, Perkins does not teach or render "obvious to try" all of the limitations of Applicant's amended claims. Using the fibrin sealant of Edwardson in the methods of Perkins might provide the skilled artisan with a method for occluding or sealing leaks in an air passage leading to the lung after collapse. Critically, however, the Applicant respectfully asserts that use of the fibrin sealant of Edwardson in the methods of Perkins would not result in or render "obvious to try" the lung volume reduction methods claimed by Applicant. Therefore, the Applicant respectfully asserts that the combination of Perkins and Edwardson does not render unpatentable any of the amended claims.

Based on the foregoing, Applicant respectfully requests withdrawal of the claim rejections under 35 U.S.C. § 103(a) based on Perkins in view of Edwardson.

Perkins in view of Edwardson and Antanavich

Claims 22-23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Perkins in view of Edwardson, and further in view of US Patent No. 5,814, 022 to Antanavich et al. ("Antanavich"). The Applicant respectfully traverses the rejection.

Again, the Applicant respectfully disagrees with the Examiner's contention that Applicant has attempted to "show non-obviousness by attacking the cited references individually where the rejection is based on a combination of references." *Office Action* at page 6. Rather, the Applicant asserts that the skilled artisan would not arrive at the claimed invention based on the combination of Perkins, Edwardson and Antanavich because the cited combination does not disclose or render "obvious to try" all of the limitations of the rejected claims.

The Applicant respectfully contends that the combination of Perkins, Edwardson, and Antanavich does not meet the legal standard for *prima facie* obviousness with respect to the amended claims. Antanavich discloses the design of an apparatus for accurately dispensing tissue sealants, one of which sealants may be "an adhesive protein solution having a fibrinogen content of from 3 to 12%." The Examiner asserts that it would have been obvious to one of skill in the art "to provide the composition of fibrinogen from 3-12%, since it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art."

The Applicant respectfully asserts that the arguably relevant contribution from Antanavich to the Examiner's obviousness rejection is the disclosure of an adhesive protein solution having a fibrinogen content from 3 to 12 %. The combination of Perkins and Edwardson, which is discussed in detail above, teaches or renders "obvious to try" only delivering a plug (made of Edwardson's fibrin sealant) to occlude an air passage leading to a region of the lung ***after*** the lung has been independently collapsed by vacuum aspiration or the application of an external force. Therefore, the combination of Perkins, Edwardson, and Antanavich does not teach or render "obvious to try" all of the limitations of the amended claims.

Based on the foregoing, Applicant respectfully requests withdrawal of the claim rejections under 35 U.S.C. § 103(a) based on Perkins in view of Edwardson and Antanavich.

Fees

The Applicants believe they have provided for all required fees in connection with the filing of this Response. Nevertheless, the Commissioner is hereby authorized to charge any additional required fees due in connection with the filing of this Response to our Deposit Account, **06-1448** reference **ATX-011.03**.

Conclusion

In view of the above amendments and remarks, it is believed that the pending claims are in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite prosecution of the above-identified application, the Examiner is urged to contact the undersigned at (617) 832-1000.

Respectfully submitted,

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